IN THE CLAIMS:

Please amend the claims as follows.

Claim 1 (Currently amended) A method of identifying a secondary drug target comprising:

(a) providing a cell having a genome, including at least one primary gene defect;

(b) effecting one or more mutations in said genome of said cell~~,at one or more secondary sites~~;

(c) selecting at least one secondary site mutation that results in a gene or protein that is non-functional and which proves lethal to said cell; and

(d) determining the ~~gene product of said lethal secondary site~~ identity of said gene or protein that is non-functional to provide a secondary drug target.

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Claim 2 (Currently amended) The method of claim 1 in which said primary gene defect is found in ~~or associated with~~ a human tumor cell.

Claim 3 (Currently amended) The method of claim 1 in which said primary gene defect is analogous or homologous to a defect found in ~~or associated with~~ a human tumor cell.

Claim 4 (Original) The method of claim 1 in which said primary gene defect results in the alteration, loss, inhibition, enhancement, or gain of a function.

Claim 5 (Original) The method of claim 4 in which said function includes the suppression of tumor growth, DNA damage checkpoint, DNA mismatch repair, nucleotide excision repair, O6-methylguanine reversal, double-strand break repair, DNA helicase function, signaling, cell cycle control or apoptosis.

Claim 6 (Original) The method of claim 5 in which said signaling function includes signal transduction, tissue growth factor signaling, autocrine loop signaling, or paracrine loop signaling.

Claim 7 (Original) The method of claim 1 in which said primary gene defect includes a defect in the gene coding for pp16, p53, ATM, MSH2, MLH1, XP-A, XP-B, MGMT, BRCA2, BRCA1, BLM, RAS, NF1, MYC, PTH, Cyclin D, Cyclin E, p27kip1, or BCL-2.

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Claim 8. Canceled herein.

Claim 9. Canceled herein.

Claim 10. (Currently amended) The method of claim 1 in which said secondary site mutation is effected within a gene selected from the group consisting of ~~ede9, ede2,~~ a gene encoding a gene product exhibiting polymerase δ exonuclease function, a gene encoding a gene product exhibiting polymerase ε exonuclease function, a gene encoding a ribonucleotide reductase, ~~mec1,~~ a rad53 - like gene, ~~ede53, ede34, ede14, ede15,~~ a gene

encoding NUP170, ~~dbf2,~~ a gene encoding CLN2, ~~rad3, rad9, rad27, cde8,~~ a gene encoding Mlu-1 box binding factor, ~~slm1,~~ a gene encoding MBF, a gene encoding PCNA, ~~or~~ and a gene encoding a replication fork protein.

Claim 11. (Currently amended) The method of claim 1 in which said secondary site mutation is effected within a gene coding for a gene product selected from PIK-related kinase ~~(mec1)~~, E2 ubiquitin carrier protein ~~(cde34)~~, E3 ubiquin ligase ~~(cde53)~~, ubiquitin ligase ~~(skp1)~~, protein phosphatase ~~(cde14)~~ and nuclear pore protein ~~(NUP170)~~.

Claim 12. (Original) The method of claim 1 in which said secondary site mutation is effected within a gene having a mammalian analog or homolog.

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Claim 13. (Original) The method of claim 12 in which said mammalian homolog is selected from the group consisting of a gene encoding a DNA ligase I, a gene encoding a DNA polymerase, a gene encoding a ribonucleotide reductase, a gene encoding a FEN-1, a gene encoding Cyclin D, a gene encoding Cyclin E, an AT-related gene, a gene encoding NUP-155 or a gene encoding an isozyme.

Claim 14. Canceled herein.

Claim 15. (Original claim) The method of claim 1 which further comprises using said secondary drug target to screen for a drug or drug candidate.

Claim 16. (Original claim) The method of claim 15 in which said drug or drug candidate interacts with, binds to, or inhibits a gene product selected from the group consisting of DNA ligase, DNA polymerase, polymerase δ exonuclease, polymerase ε exonuclease, ribonucleotide reductase, a subunit of transcriptional activator, a transcription factor, PCNA, a replication fork protein, PIK-related kinase, recombinase, E3 ubiquitin ligase, E2 ubiquitin carrier protein, a protein tyrosine phosphatase, a nuclear pore protein, cyclin, DNA repair exonuclease, thymidylate kinase, a gene product of slm 1, ribonucleottide reductase, or a transcriptional activator.

Claim 17. (Original claim) The method of claim 15 in which said drug or drug candidate inhibits the growth of a human tumor.

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Claim 18. (Currently amended) A method of rational antitumor drug design comprising: (i) providing a genetically tractable organism harboring an altered gene that is analogous or homologous to a primary tumor defect, (ii) performing a synthetic lethal screen to identify a secondary target gene, (iii) determining an analogous or homologous secondary target in mammalian cells, and (iv) using said analogous or homologous secondary target to screen for a drug or drug candidate having antitumor activity, wherein said genetically tractable organism is selected from the group consisting of *Saccharamyces cerevisiae*, *Schizzosaccaromyces pombe*, *Caenorhabditis elegans*, and *Drosophila melanogaster*.

Claim 19. (Original claim) The method of claim 18 in which the drug or drug candidate comprises a small molecule.

Claim 20. (Original claim) The method of claim 17 which further comprises validating the synthetic lethality of said analogous or homologous secondary target in a mammalian cell relative to a mammalian non-tumor cell.

Claim 21. Withdrawn

Claim 22. Withdrawn

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Claim 23. The method of claim 1 in which said primary gene defect includes a defect in a gene coding for PIK-related kinase (mec1).

Claims 24-46. Withdrawn